ELSEVIER

European Journal of Cardio-thoracic Surgery 35 (2009) 293–298

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Airway complications after lung transplantation: risk factors, prevention and outcome☆

Walter Weder [a,1,*], Ilhan Inci [a,1], Stephan Korom [a], Peter B. Kestenholz [a], Sven Hillinger [a], Christine Eich [b], Sarosh Irani [b], Didier Lardinois [a]

[a] University Hospital, Division of Thoracic Surgery, University of Zurich, Switzerland
[b] University Hospital, Division of Pulmonary Medicine, University of Zurich, Switzerland

Received 11 June 2008; received in revised form 22 September 2008; accepted 24 September 2008; Available online 11 November 2008

Abstract

Purpose: Anastomotic complications following lung transplantation (LuTx) have been described in up to 15% of patients. Challenging to treat, they are associated with high morbidity and a mortality rate of 2–5%. The aim of this study was to analyze the incidence of complications in a consecutive series of bronchial anastomosis after LuTx at our center and to delineate the potential risk factors. **Methods:** Between 1992 and 2007, 441 bronchial anastomoses were performed in 235 patients. Indications for transplantation were cystic fibrosis (35.7%) emphysema (28.1%) pulmonary fibrosis (12.8%) and pulmonary hypertension (7.7%). There were 206 sequential bilateral and 28 single transplants including lobar engraftments in 20 cases. The donor bronchus was shortened to the plane of the lobar carina including the medial wall of the intermediate bronchus. Peribronchial tissue was left untouched. Anastomosis was carried out using a continuous absorbable running suture (PDS 4/0) at the membranous and interrupted sutures at the cartilaginous part. Six elective surveillance bronchoscopies were done monthly during the first half-year post-LuTx, with detailed assessment of the pre- and post-anastomotic airways. **Results:** One-year survival since 2000 was 90.5%. In all 441 anastomoses performed, no significant dehiscence was observed. In one patient, a small fistula was detected and closed surgically on postoperative day five. Fungal membranes were found in 50% of the anastomoses at 1 month and in 14% at 6 months. Discrete narrowing of the anastomotic lumen without need for intervention was found in 4.9% of patients at 1 month and in 2.4% at 6 months. Age, cytomegalovirus status, induction therapy, immunosuppressive regimen, ischemic time, and ventilation time had no influence on bronchial healing. **Conclusions:** Clinically relevant bronchial anastomotic complications after LuTx can be avoided by use of a simple standardized surgical technique. Aggressive antibiotic and antifungal therapy might play an important supportive role.

Keywords: Airway; Anastomosis; Lung transplantation; Complications

1. Introduction

The major cause of death following pulmonary transplantation in the first 15 years after the first human lung transplantation was airway dehiscence, representing a formidable obstacle to widespread use of this novel procedure [1].

Pulmonary transplantation is unique among all solid organ transplantations, since systemic arterial blood supply is not (routinely) restored during engraftment. For this reason, anastomotic complications have primarily been attributed to ischemia of the donor bronchus [2]. Additionally rejection [3], intense immunosuppressive therapy [4], invasive infections [5], or inadequate organ preservation [2] were factors identified as being associated with compromised airway healing. Furthermore, severe reperfusion edema and early rejection episodes have been shown as independent predictors of bronchial complications [6].

Recently, refinements in lung preservation and surgical technique, improvements in patient selection, postoperative care and immunosuppression have reduced the prevalence of airway complications [7]. Reflecting these changes, the contemporary rate of anastomotic lesions following LuTx has dropped from 80% before 1983 [15] to 2.6–23.8% [6–14].

In this investigation we analyzed the incidence of airway anastomotic complications in 235 consecutive patients at our center to delineate potential risk factors.

2. Patients and methods

We reviewed the data from a consecutive series of 235 patients transplanted at our center between November 1992

☆ Presented at the 16th European Conference on General Thoracic Surgery, Bologna, Italy, June 8–11, 2008.

* Corresponding author. Address: Department of Thoracic Surgery, Raemistrasse 100, 8091 Zurich, Switzerland. Tel.: +41 44 2558802; fax: +4144 255 8805.
E-mail address: walter.weder@usz.ch (W. Weder).

[1] Walter Weder and Ilhan Inci have equally contributed to this paper.

1010-7940/$ – see front matter
doi:10.1016/j.ejcts.2008.09.035

and December 2007. The mean age of the patients was 41 years (9—69), comprising 121 females and 114 males. The indications for lung transplantation were: cystic fibrosis ($n = 84$), emphysema ($n = 66$), pulmonary fibrosis ($n = 30$), pulmonary hypertension ($n = 18$) and others ($n = 37$) (Table 1).

This series consisted of one heart—lung, 28 single lung and 206 bilateral sequential lung transplants for a total of 441 anastomoses performed using the same technique. Of this cohort 28 patients died in the hospital (in-hospital mortality 11%) and one heart—lung transplant patient was excluded from the study leaving 206 patients available for the analysis. A total of 391 anastomoses at risk in 206 patients were evaluated using elective bronchoscopy during the first 6 postoperative months. Since 2000 1-year and 5-year survival was 90.5% and 78%, respectively.

Table 1
Recipient variables (441 anastomoses in 235 patients).

Age (years)	41.8 (9—69)
Weight (kg)	58 (24—122)
Height (cm)	166.8 (133—191)
Gender	
Male	114 (48.5)
Female	121 (51.5)
Diagnosis	
Emphysema	66 (28.1)
Cystic fibrosis	84 (35.7)
IPF	30 (12.8)
PPH	18 (7.7)
Other	37 (15.7)
Preoperative steroid use	
Yes	51 (21.7)
CMV status (recipient/donor)	
neg/neg	86 (36.6)
neg/pos	56 (23.8)
pos/neg	36 (15.3)
pos/pos	57 (24.3)
Induction	
Basiliximab	132 (56.2)
ATG	13 (8.4)
Immunosuppression	
C-Az-P	62 (26.4)
C-MMF-P	173 (73.6)
Organ preservation solution	
Euro-Collins	91 (38.8)
Perfadex	144 (61.2)
Type of operation	
Unilateral transplantation	28 (11.9)
Bilateral transplantation	206 (87.8)
Heart—lung transplantation	1 (0.4)
Down-sizing	
Yes	65 (27.7)
Lobar transplantation	20 (8.5)
CRP at transplantation	18 (1—162)
Total operation time (min)	382.6 (140—970)
Ischemia time (min)	
Right lung	234.3 (62—658)
Left lung	304.7 (79—533)
Ventilation time (days)	4.8 (1—218)
ICU time (days)	11.5 (1—218)
Mortality (in-hospital)	28 (11.9)

Values are given as n (%) or mean (minimum—maximum). CRP: C reactive protein (mg/l). IPF: interstitial pulmonary fibrosis, PPH: primary pulmonary hypertension, neg: negative, pos: positive, ATG: anti-thymocyte globulin, C-Az-P: cyclosporine—azathioprine—prednisone, C-MMF-P: cyclosporine—mycophenolate mofetil—prednisone, ICU: Intensive care unit.

Euro-Collins solution was used until 2000; thereafter Perfadex (Vitrolife, Sweden) had been introduced. Before antegrade flush 500 μg prostaglandin E1 (Prostin VR, Upjohn, Puurs, Belgium) was injected into the pulmonary artery in all cases. We are also using retrograde flush with Perfadex at the time of the back-table preparation since 2000.

The surgical approach for single lung transplantation was an anterolateral thoracotomy. For bilateral sequential lung transplantation bilateral trans-sternal anterior thoracotomy (clamshell incision) or, since 2000, two separate anterolateral thoracotomies were performed.

First the bronchial anastomoses were carried out. The recipient's main bronchus was divided one ring proximal of the branching of the upper lobe bronchus. The bronchial arteries were ligated, avoiding electrocoagulation of the peribronchial tissue. All dissection close to the bronchus was done using 'minimal' or 'no touch' technique in order to keep the peribronchial tissue intact. The donor bronchus was cut back as close to the origin of the upper lobe bronchus as possible, with special attention to keep the peribronchial tissues undisturbed (Fig. 1). We consider the oblique resection of the medial (extrapulmonary) wall of the intermediate bronchus important. Absorbable suture material polydioxanone (PDS, Ethicon Inc., NJ) was used. A continuous suture of the membranous wall (PDS, 4/0) and end-to-end anastomosis with interrupted single sutures (PDS, 3/0) of the cartilaginous part was performed. The first suture to unite the cartilaginous parts was placed in the middle of the circumference to achieve optimal size matching. Forced telescoping of the anastomosis was avoided, and telescoping was employed only when it occurred spontaneously in the event of donor-to-recipient size mismatch. Only in the first three recipients of this series was the anastomosis covered with omentum. Thereafter, this technique was abandoned and peribronchial tissue was used.

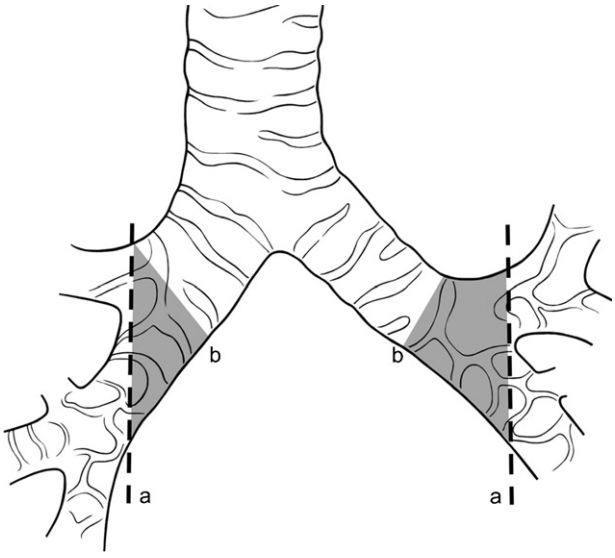

Fig. 1. Cut points on the donor bronchus. (a) The donor bronchus should be cut back as close as possible to the upper lobe bronchus origin in an oblique plane with special attention to keep peribronchial tissues undisturbed (b) If donor bronchus cut at this level there will be a risk zone for bronchial ischemia (gray zone).

The patients received regular triple immunosuppressive therapy with cyclosporine, azathioprine (since 1997 replaced by mycophenolate mofetil), prednisone and prophylaxis against pneumocystis carinii, cytomegalovirus (CMV) and fungal infections. The initial dose of methylprednisone was 1000 mg (500 mg/completed anastomosis) i.v. before reperfusion followed by 125 mg i.v. for the first postoperative day. Then the recipients received 0.5 mg/kg/day prednisone as a maintenance dose.

Antibiotic therapy was adjusted based on the antibiotic sensitivities from preoperative sampling of the recipient and the donor bronchus before implantation.

Airway status was examined with flexible bronchoscopy after completion of anastomosis during the operation. Follow-up bronchoscopies together with transbronchial surveillance biopsy were done every 3—4 weeks for the first 6 months.

Bronchial healing was assessed according to the classification of Couraud as follows: grade 1: complete primary mucosal healing; grade 2a: complete primary healing without necrosis, partial primary mucosal healing; grade 2b: complete primary healing without necrosis, no primary mucosal healing; grade 3a: limited focal necrosis (extending less than 5 mm from the anastomotic line); grade 3b: extensive necrosis [16].

Furthermore, bronchoscopic descriptions were also evaluated according to presence and extent of fungal membranes, hyperemia, and hyperplasia using a semi quantitative scale as follows: 0: none; 1: mild; and 2: severe. Luminal narrowing was defined as 10-30 luminal occlusion relative to proximal, pre-anastomotic native bronchus.

We compared the patients displaying luminal narrowing to recipients without during the first surveillance bronchoscopy. The variables assessed were age, weight, height, gender, indication for transplantation, preoperative steroid use, cytomegalovirus status, induction therapy, immunosuppression, preservation solution, type of operation, down-sizing, C reactive protein (CRP) at transplantation, total operation time, ischemia time, duration of ventilation and ICU stay.

3. Statistical analysis

All data were collected retrospectively. The statistical analysis was performed with SPSS 15.0 for Windows. To test for univariate differences in categorical variables, we used Pearson's chi-square test. For continuous variables, we used the Mann—Whitney U test. We considered $p < 0.05$ to indicate statistical significance.

4. Results

In this study, a total of 391 anastomoses at risk were evaluated. Altogether, no severe airway complications occurred, except for one patient who experienced a small anastomotic fistula directly postoperatively, which was closed surgically at day five following transplantation. In the first surveillance bronchoscopy luminal narrowing was observed in 10 patients (4.9%) (18/391 anastomoses, 4.6%). Yet, there was no clinical meaningful respiratory impairment, with no need for stenting or surgical revision. The rate of luminal narrowing decreased to 2.4% (5/206 patients) (9/391 anastomoses, 2.3%) at the sixth bronchoscopy (Table 2).

Complete primary mucosal healing based on the Couraud classification was seen in 73.3% of the anastomoses (Couraud

Table 2
Bronchoscopy details in 391 anastomoses at risk.

Bronchoscopy	1	2	3	4	5	6
Day (mean)	39.1	72.1	106.2	133.2	170.3	202.5
CRP (mean)	11.2	4.1	4.8	3.9	3.1	5.6
Fungal membrane (L; R, %)						
None	50.5; 48	48.1; 44.7	65.4; 60	68.3; 63.9	72.7; 70.2	85.4; 86.4
Mild	35; 35.9	43.1; 44.1	26.8; 32.4	28.9; 32.3	22.7; 27.3	14.1; 13.1
Severe	14.5; 16.1	8.8; 11.2	7.8; 7.6	2.8; 3.8	4.7; 2.5	0.5; 0.5
Hyperemia (L; R, %)						
None	31.7; 33.5	30.6; 31.6	44.4; 40.7	53.5; 50	57; 56.2	50.8; 55.4
Mild	47.8; 45.7	54.4; 51.3	45.1; 48.3	39.4; 43.2	37.5; 38.8	43.2; 37.5
Severe	20.6; 20.8	15; 17.1	10.5; 11	7; 6.8	5.5; 5	5.9; 7.1
Hyperplasia (L; R,%)						
None	80.2; 79.2	83.9; 86.8	86.3; 83.6	86.5; 86.5	92.2; 90.1	91.5; 92.9
Mild	17.6; 18.5	14.3; 10.6	12.4; 14.4	10.6; 11.3	6.3; 9.9	7.6; 6.3
Severe	2.2; 2.3	1.9; 2.6	1.3; 2.1	6.8; 2.3	1.6; 0	0.8; 0.9
Luminal narrowing (%)						
No	95.1	95.1	95.6	96.6	96.1	97.6
Left	1	1.9	1.0	1.0	1.4	0.5
Right	0.5	1.5	1.0	0.5	0.5	0
Bilateral	3.4	1.5	2.4	1.9	1.9	1.9
Couraud classification (%)						
1	73.3	83.9	88.3	94.2	93.7	95.2
2a	20.4	10.6	7.2	4.8	5.3	3.8
2b	5.8	4.8	3.5	1.0	0.5	1.0
3a	0.5	0.5	1.0	0	0.5	0

L: left, R: right. Bronchoscopies are evaluated using a semi quantitative scale for fungal membranes, hyperemia, and hyperplasia as follows: 0: none; 1: mild; and 2: severe. CRP: C reactive protein (mg/l).

grade 1) at first bronchoscopy, which increased to 95.2% by the end of the 6-month timeframe. Primary healing, however, displaying partial mucosal healing without necrosis (Couraud grade 2a and/or 2b) was seen in 26.2% of the anastomoses at the first bronchoscopy, which decreased to 4.8% at the sixth bronchoscopy, never requiring any treatment (Table 2).

Severe fungal membranes were found in 14.5% (left bronchus) and in 16.1% (right bronchus) of the anastomoses during the first surveillance inspection (Table 2). This was reduced to 0.5% at the sixth bronchoscopy. As a matter of fact, by 6 months, about 85% of the anastomoses were free of fungal membranes (Table 2).

There were 10 patients with luminal narrowing compared to 196 patients without. Age, weight, height, gender, diagnosis leading to transplantation, preoperative steroid use, CMV status, induction therapy, immunosuppression, type of operation, down-sizing, CRP at transplantation, total operation time, ischemia time, time on ventilator and ICU duration did not differ between the two groups (Table 3). Only type of organ preservation solution ($p = 0.04$) and lobar transplantation ($p = 0.02$) differed significantly between groups.

When we compared the first and the sixth bronchoscopies only the extent of hyperplasia, and the Couraud grading differed significantly between the two groups (for the first bronchoscopy; $p = 0.0001$, $p = 0.002$, respectively; for the sixth bronchoscopy $p = 0.0001$ and $p = 0.01$, respectively). Presence and extent of fungal membranes and hyperemia were comparable between the two time points.

Table 3
Comparison of variables between the groups with and without luminal narrowing.

	Group I ($n = 196$)	Group II ($n = 10$)	p value
Age (years)	42.2 (12–69)	43.8 (18–60)	0.79
Weight (kg)	57.2 ((24–103)	56.4 (40–75)	0.76
Height (cm)	166.8 (133–191)	167.7 (153–182)	0.85
Gender (n)			0.97
Male	98	5	
Female	98	5	
Diagnosis			0.35
Emphysema	60 (30.6)	2 (20)	
Cystic fibrosis	73 (37.2)	3 (30)	
IPF	22 (11.2)	2 (20)	
PPH	11 (5.6)	–	
Other	30 (15.3)	3 (30)	
Preoperative steroid use			0.15
Yes	42 (21.4)	4 (40)	
CMV status (recipient/donor)			0.94
neg/neg	69 (35.2)	4 (40)	
neg/pos	53 (27)	2 (20)	
pos/neg	28 (14.3)	2 (20)	
pos/pos	47 (23.9)	2 (20)	
Induction			
Basiliximab	111 (56.6)	7 (70)	0.24
ATG	13 (13.5)	–	0.40
Immunosuppression			0.63
C-Az-P	47(23.9)	1 (10)	
C-MMF-P	149 (76.1)	9 (90)	
Organ preservation solution			
Euro-Collins	78 (39.7)	7 (70)	0.04
Perfadex	118 (60.3)	3 (30)	
Type of operation			0.33
Unilateral transplantation	19 (9.7)	2 (20)	
Bilateral transplantation	177 (90.3)	8 (80)	
Down-sizing			
Yes	56 (28.5)	2 (20)	
Lobar transplantation	17 (8.6)	1 (10)	0.02
CRP at transplantation	17.2(1–138)	18.4(1–58)	0.69
Total operation time (min)	379 (140–620)	335 (205–435)	0.30
Ischemia time (min)			
Right lung	232 (65–475)	237.3 (162–335)	0.70
Left lung	306 (111–533)	269 (79–379)	0.38
Ventilation time (day)	2.7 (1–75)	1.2 (1–3)	0.23
ICU time (day)	9.04 (1–142)	10.5 (2–29)	0.44

Values are given as n (%) or mean (minimum–maximum). Group I: patients without luminal narrowing at the first bronchoscopy, group II: patients with luminal narrowing at the first bronchoscopy. CRP: C reactive protein (mg/l). IPF: interstitial pulmonary fibrosis, PPH: primary pulmonary hypertension, neg: negative, pos: positive, ATG: anti-thymocyte globulin, C-Az-P: cyclosporine–azathioprine–prednisone, C-MMF-P: cyclosporine–mycophenolate mofetil–prednisone, ICU: Intensive care unit.

5. Discussion

In all 441 anastomoses performed, no significant dehiscence was observed. In one patient, a small fistula was detected and closed surgically on postoperative day five. In only 4.9% (10/206) of recipients luminal narrowing was found at the first surveillance bronchoscopy in a consecutive series of 391 bronchial anastomoses (4.6%, 18/391). This rate decreased to 2.3% (9/391) after 6 months. None of these patients required any intervention, and there was no death related to bronchial anastomotic complications.

Bronchial ischemia is reported to be a significant risk factor for the development of airway complications [9]. The viability of the donor bronchus is initially dependent upon retrograde low-pressure collaterals derived from the pulmonary artery as bronchial arterial circulation is lost during the harvest of the donor lungs [3]. Several techniques have been proposed to protect the bronchial anastomosis: keeping the donor bronchus as short as possible and wrapping the anastomosis with vascularized pedicles [2], direct revascularization of donor bronchial arteries [17], and double antegrade and retrograde flush perfusion of the donor lungs at the time of harvest [18].

Based on the favorable results from animal studies, routine use of bronchial anastomotic omentopexy (omentum wrapping) in the early days of lung transplantation was thought to be a key strategy to overcome bronchial healing problems by enhancing the microcirculation of the donor bronchus [7]. This technique, although widely used then, has been shown to be no longer essential [19]. We, like other transplant centers, also used omentopexy initially, but then abandoned this method. Another strategy aimed at avoiding perioperative steroids as they were believed to negatively influence the healing process. However, prevention of rejection and potential amelioration of reperfusion injury are useful effects of steroids [20]. During acute rejection episodes, microcirculation may be significantly impaired due to an increase in pulmonary vascular

resistance and decrease in pulmonary collateral blood supply [21].

Combined parenteral administration of heparin and prostaglandin early in the postoperative period has been advocated in order to increase microcirculation and retrograde perfusion to the donor bronchus [19]. In our series all donor lungs were preserved with prostaglandin E1 injected into the main pulmonary artery before starting with cold antegrade perfusion of pulmonary preservation solution. Heparin is started 6 h postoperatively with 5000 IU/24 h and increased gradually to 10,000 and further to 15,000 IU/24 h continuous i.v. infusion depending on the clinical picture. We do not employ prostaglandins in the postoperative period.

Recently, severe reperfusion injury and early rejection episodes have been demonstrated to be independent predictors of bronchial complications [6]. We and other investigators have demonstrated that the number of acute rejection episodes was not related to the occurrence of bronchial complications [7,9,22].

A strong correlation between the intrabronchial presence of *Aspergillus* and the incidence of airway complications has been reported [11]. When bronchial necrosis was described at the first postoperative bronchoscopy together with *Aspergillus* infection, the incidence of later airway complications was higher than if there was necrosis alone. In our protocol we start with antifungal therapy early postoperatively using nebulized amphotericin B (2×10 mg/day) and per oral itraconazole (2×200 mg/day). Our findings support this approach as nearly 85% of the patients did not have fungal membranes at their 6th bronchoscopy. In addition the rate of severe fungal membranes decreased from 15% to 0.5%. This, in part, may explain the low incidence of airway complications in the present series.

We firmly believe that the surgical technique is paramount for the future successful healing of the bronchial anastomosis. The surgical approach for performing the anastomosis may vary among transplant centers. Telescoping, end-to-end anastomosis with a running suture for the membranous part and interrupted sutures for the cartilaginous part, and end-to-end anastomosis with a single running suture are most often used [7,9,12,22]. Some centers have reported changing their anastomotic technique from telescoping to end-to-end single suture, due to a high airway complication rate [12,13]. Others have employed telescoping or a modified telescoping technique from the beginning of their program with a low complication rate [8,9]. In fact, in most of the studies telescoping has been demonstrated to be an independent risk factor for airway complication [7,13,14]. We have not modified our technique since our program was established in 1992. Furthermore, we think that resection of the donor bronchus down to the lobar carina in an oblique plane (Fig. 1), in conjunction with keeping the peribronchial tissue intact is a critical step while performing the bronchial anastomosis.

The often cited disadvantages for a single-stitch-technique compared to a running suture, more time required, a higher load of foreign tissue due to the necessity to tie multiple knots and an overall increased tissue irritation, do not reflect our experience.

There is no standardized internationally accepted classification scheme to assess airway healing [11,12,16]. Couraud et al. [16] graded airway healing based on the bronchoscopic appearance, showing a good correlation with the subsequent development of anastomotic sequel. This grading system ranges from perfect mucosal healing (grade 1) to extensive necrosis (grade 3b). In their report the incidence of anastomotic complications significantly differed between grades 3a and 3b compared to grades 1, 2a and 2b. We also used Couraud classification to assess airway healing in our series. In the first bronchoscopy we detected a significant difference between the groups without luminal narrowing and with luminal narrowing. This observation is in accordance with the original report demonstrating high incidence of airway complications in grades 3a and 3b compared to grades 1, 2a and 2b [16].

In conclusion, our data demonstrate that bronchial anastomotic complications can be avoided by use of a standardized surgical technique, which respects the fact that the donor bronchus is poorly vascularized. Prevention of fungal infections with aggressive antifungal treatment may play an important additive role.

References

[1] Veith FJ, Kamholz SL, Mollenkopf FP, Montefusco CM. Lung transplantation. Transplantation 1983;35:271–8.

[2] Shennib H, Massard G. Airway complications in lung transplantation. Ann Thorac Surg 1994;57:506–11.

[3] Takao M, Katayama Y, Onoda K, Tanabe H, Hiraiwa T, Mizutani T, Yada I, Namikawa S, Yuasa H, Kusaqawa M. Significance of bronchial mucosal blood flow for the monitoring of acute rejection in lung transplantation. J Heart Lung Transplant 1991;10:956–67.

[4] Lima O, Cooper JD, Peters WJ, Ayabe H, Townsend E, Luk SC, Goldberg M. Effects of methylprednisolone and azathioprine on bronchial healing following lung autotransplantation. J Thorac Cardiovasc Surg 1981;82:211–5.

[5] Kshettry VR, Kroshus TJ, Hertz MI, Hunter DW, Shumway SJ, Bolman IIIRM. Early and late complications after lung transplantation: incidence and management. Ann Thorac Surg 1997;63:1576–83.

[6] Ruttmann E, Ulmer H, Marchese M, Dunst K, Geltner C, Margreiter R, Laufer G, Mueller LC. Evaluation of factors damaging the bronchial wall in lung transplantation. J Heart Lung Transplant 2005;24(March (3)):275–81.

[7] Date H, Trulock EP, Arcidi JM, Sundaresan S, Cooper JD, Patterson GA. Improved airway healing after lung transplantation. An analysis of 348 bronchial anastomoses. J Thorac Cardiovasc Surg 1995;110(November (5)):1424–32.

[8] Schroder C, Scholl F, Daon E, Goodwin A, Frist WH, Roberts JR, Christian KG, Ninan M, Milstone AP, Loyd JE, Merrill WH, Pierson III RN. A modified bronchial anastomosis technique for lung transplantation. Ann Thorac Surg 2003;75(June (6)):1697–704.

[9] Alvarez A, Algar J, Santos F, Lama R, Aranda JL, Baamonde C, Lopez-Pujol J, Salvatierra A. Airway complications after lung transplantation: a review of 151 anastomoses. Eur J Cardiothorac Surg 2001;19(April (4)):381–7.

[10] Choong CK, Sweet SC, Zoole JB, Guthrie TJ, Mendeloff EN, Haddad FJ, Schuler P, De la Morena M, Huddleston CB. Bronchial airway anastomotic complications after pediatric lung transplantation: incidence, cause, management, and outcome. J Thorac Cardiovasc Surg 2006;131(January (1)):198–203.

[11] Herrera JM, McNeil KD, Higgins RS, Coulden RA, Flower CD, Nashef SA, Wallwork J. Airway complications after lung transplantation: treatment and long-term outcome. Ann Thorac Surg 2001;71(March (3)):989–93. discussion 993–4.

[12] Aigner C, Jaksch P, Seebacher G, Neuhauser P, Marta G, Wisser W, Klepetko W. Single running suture–the new standard technique for bronchial anastomoses in lung transplantation. Eur J Cardiothorac Surg 2003;23(April (4)):488–93.

[13] Murthy SC, Blackstone EH, Gildea TR, Gonzalez-Stawinski GV, Feng J, Budev M, Mason DP, Pettersson GB, Mehta AC. Impact of anastomotic

airway complications after lung transplantation. Ann Thorac Surg 2007;84(August (2)):401—9.
[14] Van De Wauwer C, Van Raemdonck D, Verleden GM, Dupont L, De Leyn P, Coosemans W, Nafteux P, Lerut T. Risk factors for airway complications within the first year after lung transplantation. Eur J Cardiothorac Surg 2007;31(April (4)):703—11.
[15] Wildevuur CRH, Benfield JR. A review of 23 human lung transplants by 20 surgeons. Ann Thorac Surg 1970;9:489—515.
[16] Couraud L, Nashef SA, Nicolini P, Jougon J. Classification of airway anastomotic healing. Eur J Cardiothorac Surg 1992;6:496—7.
[17] Baudet EM, Dromer C, Dubrez J, Jougon JB, Roques X, Velly J-F, Deville C, Couraud L. Intermediate-term results after en bloc double-lung transplantation with bronchial arterial revascularization. J Thorac Cardiovasc Surg 1996;112:1292—300.
[18] Alvarez A, Salvatierra A, Lama R, Algar J, Cerezo F, Santos F, Baamonde C, Pujol JL. Preservation with a retrograde second flushing of Eurocollins in clinical lung transplantation. Transplant Proc 1999;31:1088—90.
[19] Shafers HJ, Haverich A, Wagner TO, Wahlers T, Alken A, Borst HG. Decreased incidence of bronchial complications following lung transplantation. Eur J Cardiothorac Surg 1992;6:174—9.
[20] Novick RJ, Menkis AH, McKenzie FN, Reid KR, Pflugfelder PW, Kostuk WJ, Ahmad D. The safety of low dose prednisone before and immediately after heart—lung transplantation. Ann Thorac Surg 1991;51:642—5.
[21] Calhoon JH, Grover FL, Gibbons WJ, Bryan CL, Levine SM, Bailey SR, Nichols L, Lum C, Trinkle JK. Single lung transplantation. Alternative indications and technique. J Thorac Cardiovasc Surg 1991;101:816.
[22] Schmid RA, Boehler A, Speich R, Frey HR, Russi EW, Weder W. Bronchial anastomotic complications following lung transplantation: still a major cause of morbidity? Eur Respir J 1997;10(December (12)):2872—5.

Appendix A. Conference discussion

Dr D. Van Raemdonck (*Leuven, Belgium*): I may have missed it, but I did not see any slide on the indications for lung transplantation in your center. Our group reported our bronchial complications at this meeting two years ago in Stockholm (Van De Wauwer C et al. Eur J Cardiothorac Surg 2007;31:703—710) and we found that especially in tall emphysema recipients we had more bronchial complications than in other patients, and this has also been reported by other groups. Can you tell us how many emphysema patients you transplanted and whether this could have influenced your good results?

Dr Inci: In our center the most common indication is cystic fibrosis followed by COPD. So about 27% of our patients have chronic obstructive pulmonary diseases, including alpha-1 antitrypsin deficiency. This was on the slide, but I didn't write the numbers, I mentioned just as a percentage, as a second highest percentage. I also evaluated in univariate analysis the height of the recipients also, but this was not significant.

Dr G.A. Patterson (*St. Louis, MO*): Can I ask a technical question. I have an idea that a significant explanation for the low risk of ischemia is how very short you make the donor airway, particularly on the right, and if that donor airway division extends into the bronchus intermedius, it seems to me that the hilum of the right lung is going to have to be elevated significantly. Having the donor lung so high, does that in any way complicate either the arterial or the venous anastomosis?

Dr Inci: We cut obliquely up to the upper lobe, but we do not shorten the intermediate bronchus too much. In an oblique plane, we leave the membranous part may be a little bit longer than shown in the slide. And so after the anastomosis, we do not see any problem with the arterial or venous anastomosis.

Dr H. Kara (*Istanbul, Turkey*): My question is about the application of steroids to the donor. Do you believe that giving steroids to the donor would affect the success of the stump after transplantation?

Dr Inci: During the early days of transplantation, this issue was a little bit of concern. When you check the papers published they wanted to avoid giving steroids to the donors in order to have a good healing in the airways, and then after data from St. Louis and other centers, they saw that it does not have a negative effect on healing, plus they are given steroids for prevention of rejection and ischemia-reperfusion injury. In addition when you have an ischemia-reperfusion injury you have a construction of the collaterals on the bronchus so you have low perfusion, and you need these collaterals in order for the healing of the anastomosis. We now allow the patients with steroids, and donor steroids also, and perioperatively we give 500 mg to each side after we finish the anastomosis. So 1000 mg methylprednisolone for each patient, and then we continue with the steroids.